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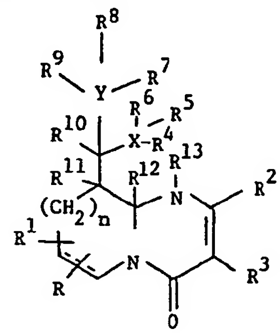
(54) Nitrogen bridgehead compounds

(57) Compounds of the general formula



I

[wherein R and R^1 are H or C_{1-4} alkyl.
or together form —(CH=CH)—$_2$,
R^2 is H or C_{1-4} alkyl
R^3 is H, C_{1-4} alkyl, phenyl, carboxy or salt thereof, alkoxycarbonyl, carbamoyl, cyano,
$—CO—NH—CO—SO_2—C_6H_4—p—CH_3$ or $—(CH_2)_s—COOR^{14}$
(s is 1, 2 or 3 and R^{14} is H or C_{1-4} alkyl,
n is 0 or 1,
(a) if R^{13} is H, and R^{12}–R^{11} and R^9–R^{10} form bonds then YR^7R^8 represents oxygen or sulfur, or
Y represents nitrogen,
R^7 is C_{1-4} alkyl, optionally substituted C_{6-10} aryl or C_{7-12} aralkyl,
R^8 is a lone pair of electrons or C_{1-4} alkyl and in this latter case a salt is formed; and
$XR^4R^5R^6$ represents halogen; or
XR^5R^6 represents oxygen or sulfur,
and R^4 is H or C_{1-4} alkyl,
XR^6 represents nitrogen and
R^4 is chloroacetyl, C_{1-4} alkyl or optionally substituted C_{6-10} aryl or heteroaryl and
R^5 is H or alkyl or
(b) if R^{11} is H and R^9–R^{10} and R^{12}–R^{13} form bonds, then
R^4, R^5, R^6, R^7, R^8, X and Y are as defined in item (a) and
(c) if R^{10}–R^{11} and R^{12}–R^{13} form bonds, then
$YR^7R^8R^9$ represents an oxygen or sulfur anion
or YR^8R^9 represents oxygen or sulphur and
R^7 is H or C_{1-4} alkyl; or
YR^9 represents nitrogen,
R^7 is H, C_{1-4} alkyl or optionally substituted C_{6-10} aryl, and
R^8 is C_{1-4} alkyl,
and $XR^4R^5R^6$ represents halogen or an oxygen or sulfur anion or XR^5R^6 is O or S and R^4 is H or C_{1-4} alkyl, or
XR^6 represents nitrogen,
R^4 is chloroacetyl, C_{1-4} alkyl or optionally substituted C_{6-10} aryl or heteroaryl and
R^5 is H or C_{1-4} alkyl, and if YR^8R^9 and XR^5R^6 each represent oxygen or sulfur or if YR^9 and XR^6 each represent nitrogen (R^5 and R^8 each being H or C_{1-4} alkyl), then
R^4 and R^7 together form optionally substituted $—(CH_2)—_s$ (s is 1, 2, 3 or 4)] and the tautomers and salts thereof. The compounds have physiological activity.

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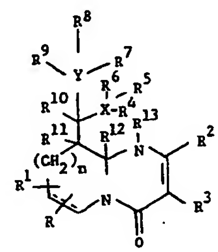
SPECIFICATION

Nitrogen bridgehead compounds, the salts thereof, processes for their preparation and pharmaceutical compositions containing them

The present invention relates to new nitrogen bridgehead compounds, the salts thereof, processes for their preparation and pharmaceutical compositions containing them.

It has been disclosed that 2-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine-9-carboxylic acid derivatives may be prepared by catalytic hydrogenation of the corresponding unsaturated compounds (J. Het. Chem. A 1499—77/330 KY *13*, 797/1976).

According to one feature of the present invention there are provided compounds of the general formula



[wherein

R represents hydrogen or C_{1-4} alkyl,

R^1 represents hydrogen or C_{1-4} alkyl and

R and R^1 together may form a $-(CH{\equiv}CH)_2$ group being attached to the two adjacent ring carbon atoms and the dotted line represents a carbon-carbon bond,

R^2 represents hydrogen, C_{1-4} alkyl,

R^3 represents hydrogen, C_{1-4} alkyl, phenyl, carboxy or salt thereof, alkoxycarbonyl containing 1—6 carbon atoms in alkoxy moiety, carbamoyl, cyano, $-CO-NH-CO-SO_2-C_6H_4-p-CH_3$ or $-(CH_2)_s-COOR^{14}$ (wherein s is 1, 2 or 3 and R^{14} represents hydrogen or C_{1-4} alkyl,

n represents 0 or 1,

(a) if R^{13} represents hydrogen and R^{12} and R^{11} together and R^9 and R^{10} together each form a chemical bond then Y represents an oxygen or sulfur atom without their lone pairs of electrons in which case R^7 and R^8 each represent a lone pair of electrons; or

Y represents a nitrogen atom without its lone pair of electrons,

R^7 represents C_{1-4} alkyl, optionally substituted C_{6-10} aryl or C_{7-12} aralkyl,

R^8 represents a lone pair of electrons or C_{1-4} alkyl and in this latter case a salt is formed with the positive nitrogen atom; and

X, R^4, R^5, R^6 together represent halogen; or

X represents an oxygen or sulfur atom without their lone pairs of electrons,

R^4 represents hydrogen or C_{1-4} alkyl,

R^5 and R^6 each represent an unshared lone pair of electrons; or

X represents a nitrogen atom without its lone pair of electrons and

R^4 represents chloroacetyl, C_{1-4} alkyl, optionally substituted C_{6-10} aryl or optionally substituted heteroaryl,

R^5 represents hydrogen or alkyl and R^6 represents a lone pair of electrons; or

(b) if R^{12} and R^{13} together form a chemical bond, R^{11} represents hydrogen and R^9 and R^{10} together form a chemical bond, then

R^4, R^5, R^6, R^7, R^8, X and Y are as defined in item (a) and

(c) if together and R^{12} and R^{13} together each form a chemical bond, then

Y represents an oxygen or sulfur atom without its lone pairs of electrons and if R^7, R^8 and R^9 each represent an unshared lone pair of electrons, then a positive cation forms a salt with the thus formed anion, or

R^8 and R^9 each represent an unshared lone pair of electrons, and

R^7 represents hydrogen or C_{1-4} alkyl; or

Y represents a nitrogen atom without its one pair of electrons,

R^7 represent hydrogen, C_{1-4} alkyl or optionally substituted C_{6-10} aryl,

R^8 is C_{1-4} alkyl, and

R^9 represents a lone pair of electrons; and

X, R^5, R^6, R^7 together represent halogen; or

X represents an oxygen or sulfur atom without their lone pairs of electrons and if R^4, R^5 and R^6 represent a lone pair of electrons, then a positive cation forms a salt with the thus formed anion, or

R^4 represents hydrogen or C_{1-4} alkyl, and

R^5 and R^6 each represent an unshared lone pair of electrons; or

X represents a nitrogen atom without its lone pair of electrons and R^4 represents chloroacetyl, C_{1-4} alkyl, optionally substituted C_{6-10} aryl or optionally substituted heteroaryl,

R^5 represents hydrogen or C_{1-4} alkyl, and

R^6 represents an unshared lone pair of electrons;

and if Y and X each represent an oxygen or sulfur atom without their lone pairs of electrons and R^5, R^6, R^7, R^8 and R^9 each represent a lone pair of electrons or if

Y and X each represent a nitrogen atom without its lone pair of electrons and R^6 and R^9 each represent a lone pair of electrons, R^5 and R^8 each represent hydrogen or C_{1-4} alkyl, then

R^4 and R^7 together form an optionally substituted $-(CH_2)-_s$ group (wherein s is 1, 2, 3 or 4)] and the tautomers and salts thereof.

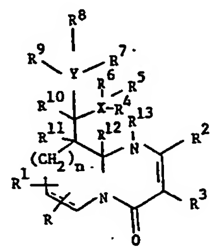
The compounds of the present invention serve as intermediates of interest in the preparation of physiologically active compounds. Compounds of the present invention also possess physiological activity *per se*.

The salts for use in pharmaceutical compositions are the physiologically compatible salts. Other salts may however be used in the preparation of the compounds of formula I and the physiologically compatible salts thereof.

Preferred compounds according to the present invention include compounds of formula I wherein n is 1 and the salts thereof. Compounds of formula I wherein R represents hydrogen and the salts thereof are also preferred. Compounds of formula I wherein R^1 represents hydrogen or C_{1-4} alkyl especially methyl and the salts are also preferred. R^2 preferably represents hydrogen.

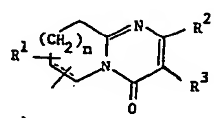
Where R^3 represents a salt of a carboxy group the salt is advantageously an alkali metal salt. Compounds of formula I wherein R^3 represents carboxy, methoxy, carbonyl, ethoxycarbonyl or carbamoyl are also preferred.

The invention further provides processes for the preparation of the compounds of the general formula



I

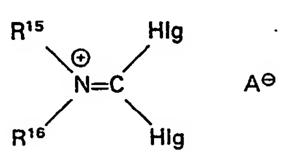
wherein the substituents are as defined above, optically active antipodes and salts thereof — comprising reacting a nitrogen bridgehead compound of the general formula



II

wherein R, R^1, R^2, R^3, n and the dotted line are as defined above,

a_1) with a dihalogeno methylene ammonium halide of the general formula



III

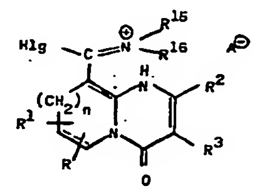
wherein

Hlg stands for halogen,

R^{15} stands for C_{1-4} alkyl, optionally substituted C_{6-10} aryl,

R^{16} stands for C_{1-4} alkyl or

A stands for an anion, obtaining thus a nitrogen bridgehead compound of the general formula



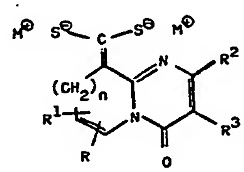
Ia

— wherein R, R^1, R^2, R^{15}, R^{16}, A, n and the dotted line are as defined above — or

a_2) with a carbon disulfide of the formula

$$CS_2 \qquad IV$$

preferably in the presence of alkali ions and obtaining thus compounds of the general formula



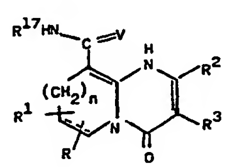
Ib

— wherein R, R^1, R^2, R^3, n, Hlg and the dotted line are as given above, and M stands for alkali ion — or

a_3) with an isocyanate of the general formula

$$R^{17}—N{=}C{=}V \qquad V$$

— wherein R^{17} stands for C_{1-4} alkyl, chloroacetyl, optionally substituted C_{6-10} aryl or optionally substituted hetaryl, V stands for oxygen or sulfur — and obtaining thus a compound of the general formula



Ic

— wherein R, R^1, R^2, R^3, R^{17}, V, n and the dotted line are as defined above —

and converting any of the compounds of the general formulae Ia, Ib, Ic obtained by any of the process variants, if desired, to a different compound of the general formula Ia, Ib, Ic or I and converting a substituent R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13}, X or Y in the obtained compound of the general formula I, if desired, into another R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13}, X or Y in an optional order and/or converting it to a pharmaceutically acceptable salt or setting it free from its salt and/or resolving, if desired, the racemate of the general formula I.

We have unexpectedly found that compounds of the general formula II contain active hydrogens in the methylene group which is in beta position related to the nitrogens and these active hydrogens are suitable for electrophilic substitution reactions. Part of the compounds of the general formula I exhibit valuable biological activity and another part serve as starting materials for the preparation of valuable biologically active compounds, thus nitrogen bridgehead compounds of the general formula I and further developed derivatives thereof may be used in therapy.

The prepared compounds of the general formula I may exist in three tautomeric forms:

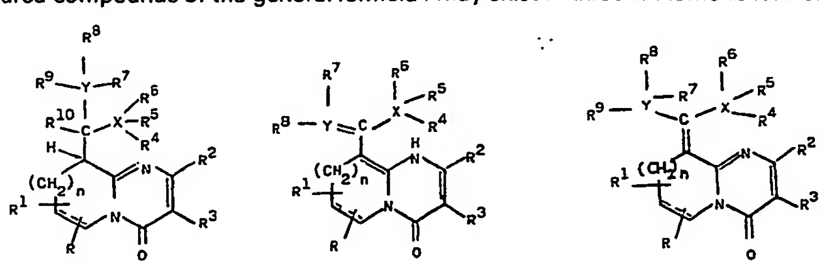


Figure 1

Depending upon the nature of the substituents one or another tautomeric form may predominate or two tautomer forms under given circumstances may form an equilibrium mixture which may be shown by spectroscopic methods. Each tautomeric form may exist in the form of Z—E geometric isomers too. In the Examples the prepared products are named considering the prevailing form.

The present invention includes the possible geometric isomers and racemic and optically active forms of the nitrogen bridgehead compounds of the general formula I.

When working according to process variant a_1) the nitrogen bridgehead compound of the general formula II is added to a solution of dihalogeno methylene ammonium halide in an inert solvent, the compound of the general formula II may be dissolved, if desired, in an inert solvent, and the reaction is completed by heating. The formed nitrogen bridgehead compound of the general formula Ia is preferably isolated by evaporating the reaction mixture followed by crystallization of the residue.

The reaction of the process variant a_1) is carried out in an inert solvent, such as hydrocarbons, preferably in benzene, toluene, xylene or chlorinated hydrocarbons, such as chloroform, dichloromethane, chlorobenzene, etc. The reaction is carried out at 0—180°C, preferably at 10—120°C. The formed compound of the formula Ia may be converted to a compound of the general formula I by reacting it for example with an amine, without isolation.

The process variant a_2) is preferably carried out by adding dropwise an alcoholic solution of alkali hydroxide under mild external cooling to an alcoholic solution of the nitrogen bridgehead compound of the general formula II and carbondisulfide of the formula IV and stirring the reaction mixture preferably at room temperature. The compounds of the general formula Ib formed in the reaction are recovered, if desired, by removing the solvent at reduced pressure. According to another preferable embodiment of the process variant the formed compound of the general formula Ib is converted to a compound of the general formula I without isolation by using, for example alkylating agents.

As alcohols preferably methanol, ethanol, n- or isopropanol or n-butanol may be employed. As alkali hydroxides sodium or potassium hydroxide is preferred. The reaction is preferably carried out at 0 to 120°C. To 1 mole of nitrogen bridgehead compound of the general formula II 1 to 5 moles of carbon disulfide of the formula IV are used.

According to process variant a_3) the nitrogen bridgehead compound of the general formula II may be reacted with an isocyanate of the general formula V without any solvent or in the presence of an inert solvent. If a solvent is used the formed compound of the general formula Ic is precipitating from the reaction mixture and may be removed by filtration. If the formed compound of the general formula Ic does not precipitate from the reaction mixture then the mixture is evaporated at a reduced pressure and the obtained residue is recrystallized from a suitable solvent. If the reaction is carried out without solvent, the reaction mixture is crystallized from a suitable solvent when the reaction is completed. The reaction is carried out at 0—250°C. The reaction temperature depends on the starting materials.

To 1 mole of nitrogen bridgehead compound of the general formula II 1 to 3 moles of the isocyanate of the general formula V are used.

A given compound of the general formula I — wherein R, R^1, R^2, R^3, n and the dotted line are as given above, R^{10} and R^{11} and R^{12} and R^{13} together form a chemical bond, X and Y stand for sulfur and R^4, R^5, R^6, R^7, R^8, R^9 represent an unshared electron-pair and an alkali metal cation forms a salt with the forming anion — is reacted

a) with an alkylating agent, thus a compound of the general formula I is obtained — wherein R, R^1, R^2, R^3, n and the dotted line are as defined above, R^9 and R^{10} and R^{11} and R^{12} together form a chemical bond, R^{13} stands for hydrogen, X and Y stand for sulfur, R^5, R^6, R^7 and R^8 represent an unshared electron-pair, R^4 stands for C_{1-4} alkyl. As alkylating agents alkyl halides, such as methyl iodide, ethyl bromide, etc., aralkyl halides, such as benzyl chloride, dialkylsulfates, such as dimethylsulfate, diethylsulfate, trialkylphosphates, such as triethylphosphate, benzene sulfonic acid and p-toluene-sulfonic acid alkyl esters, trialkyl oxonium fluoroborates, such as other usual reactants may be used. The reaction is preferably carried out in the presence of a solvent at 0 to 160°C. As solvents the usual solvents are employed, which are used in alkylation or aralkylation reactions. To 1 mole of starting material of the general formula I preferably 0.3—2.0 mole of alkylating or aralkylating agent is used depending on the nature of the used alkylating or aralkylating agent. The molar ratio of the reactants may be changed, if desired.

b) with an alkylene halide and thus compounds of the general formula I are obtained — wherein R, R^1, R^2, R^3, n and the dotted line are as defined above, R^{10} and R^{11} and R^{12} and R^{13} together form a chemical bond, X and Y stand for sulfur and R^5, R^6, R^8, R^9 stand for a lone electron-pair and R^4 and R^7 together form $-(CH_2)_s$ wherein s stands for 1, 2, 3 or 4.
The reaction may preferably be carried out under the circumstances mentioned under item a).

A given compound of the general formula I — wherein R, R^1, R^2, R^3, n and the dotted line are as given above, and R^9 and R^{10} and R^{11} and R^{12} together form a chemical bond, R^{13} represents hydrogen, X and Y represent sulfur, R^5, R^6, R^7, R^8 stand for a lone electron-pair, R^4 is a C_{1-4} alkyl, C_{7-12} aralkyl, is

a) reacted with an alkylating agent, preferably in the presence of an acid binding agent and thus such compounds of the general formula I are obtained — wherein R, R^1, R^2, R^3, n and the dotted line are as given above, R^{10} and R^{11} and R^{12} and R^{13} together form a chemical bond, X and Y stand for sulfur and R^5, R^6, R^8 and R^9 represent an unshared electron-pair, R^4 and R^7 stand for identical or different

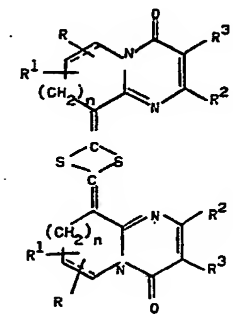
C_{1-4} alkyl.

As alkylating agents the same agents may be used as mentioned above. As acid binding agents alkali carbonate, alkali hydrogen carbonate, alkali hydroxide, trialkylamine, alkali earth metal carbonate, etc. are preferred.

The reaction is preferably carried out in the presence of a solvent.

The reaction is carried out under circumstances given above.

b) heated with acid anhydride and forming thus a 1,3-dithiethane ring from two alkyl-S—C=S groups or an aralkyl-S—C=S group and obtaining thus a compound of the general formula



Id

wherein R, R^1, R^2, R^3, n and the dotted line are as defined above. As acid anhydrides preferably aliphatic acid anhydrides, such as acetic acid anhydride, propionic acid anhydride may employed. The reaction is preferably carried out at the boiling point of the acid anhydride.

c) reacted with a diamine and obtaining thus such a compound of the general formula I — wherein R, R^1, R^2, R^3, n and the dotted line are as defined above, R^{10} and R^{11} and R^{12} and R^{13} together form a chemical bond, X and Y stand for a stripped nitrogen, atom, R^6 and R^9 represent an unshared electron-pair, R^5 and R^8 stand for hydrogen or C_{1-4} alkyl, R^4 and R^7 together form an optionally substituted —$(CH_2)_s$ group, wherein s stand for 1, 2, 3 or 4.

A given compound of the general formula I — wherein R, R^1, R^2, R^3, n and the dotted line are as defined above, R^9 and R^{10} and R^{11} and R^{12} together form a chemical bond R^{13} stands for hydrogen, X (R^4, R^5, R^6) stands for halogen, Y stands for a stripped nitrogen, R^7 is a C_{1-4} alkyl, optionally substituted C_{6-10} aryl, R^8 stands for C_{1-4} alkyl and a halide ion forms a salt with the positive nitrogen — is

a) reacted with alcohol in the presence of an alkali alkanoate and thus such compounds of the general formula I are obtained, wherein R, R^1, R^2, R^3, n and the dotted line are as defined above, R^{13} stands for hydrogen, R^9 and R^{10} and R^{11} and R^{12} form a chemical bond, X and Y stand for a stripped oxygen, R^5, R^6, R^7, R^8 stand for a lone electron-pair, R^4 is C_{1-4} alkyl.

As alcohols aliphatic or aralkyl alcohols may be used. As alkali alkanoate salts of alkali metals with aliphatic carboxylic acids are preferred. Sodium acetate and calcium acetate may also be employed. The reaction is preferably carried out at a temperature between 0 to 150°C.

b) reacted with water containing alcohol and thus such compounds of the general formula I are obtained, wherein R, R^1, R^2, R^3, n and the dotted line are as defined above, R^{13} stands for hydrogen, R^9 and R^{10} and R^{11} and R^{12} form a chemical bond, X stands for a stripped nitrogen, Y stands for a stripped nitrogen atom and R^6, R^7 and R^8 represent an unshared electron-pair, R^4 stands for a C_{1-4} alkyl, optionally substituted C_{6-10} aryl, R^5 stands for C_{1-4} alkyl.

As alcohols preferably aliphatic alcohols are used. The reaction may be carried out at 0 to 150°C, preferably at the boiling point of the used alcohol.

c) reacted with a primary or secondary amine preferably in the presence of an inert solvent and thus such compounds of the general formula I are obtained — wherein R, R^1, R^2, R^3, n and the dotted line are as given above, R^9 and R^{10}, R^{11} and R^{12} form a chemical bond, R^{13} stands for hydrogen, X and Y represent a stripped nitrogen atom, R^4 stands for C_{1-4} alkyl, optionally substituted C_{6-10} aryl, optionally substituted heteroaryl, R^5 stands for hydrogen, C_{1-4} alkyl, R^6 represents an unshared electron-pair, R^7 stands for C_{1-4} alkyl, optionally substituted C_{6-10} aryl, R^8 stands for C_{1-4} alkyl and a halide ion forms a salt with the positive nitrogen and the base is set free from the obtained salt if desired, and thus such compounds of the general formula I are obtained, wherein R, R^1, R^2, R^3, n and the dotted line are as defined above, R^{10} and R^{11} and R^{12} and R^{13} together form a chemical bond, X and Y represent a stripped nitrogen atom, R^4 stands for hydrogen, C_{1-4} alkyl, optionally substituted C_{6-10} aryl or optionally substituted heteroaryl, R^5 stands for hydrogen or C_{1-4} alkyl or R^7 stands for C_{1-4} alkyl, optionally substituted C_{6-10} aryl, R^8 represents C_{1-4} alkyl and R^6 and R^9 represent an unshared electron-pair. The reaction may be carried out at 0 to 160°C, preferably at the boiling point of the used inert solvent.

As inert solvents aromatic hydrocarbons, such as benzene, toluene, etc. halogenated hydrocarbons,

such as dichloromethane, chloroform, carbon-tetrachloride, chlorobenzene, etc. may be used.
1 to 5 moles, preferably 1.9—2.9 moles of ammonia or amine may be used related to 1 mole of the starting nitrogen bridgehead compound.
The obtained nitrogen bridgehead compound of the general formula I may be set free by using carbonates, alkali hydrogen carbonate, alkali hydroxide or trialkylamine.

d) reacted with a diamine preferably in the presence of an inert solvent and thus such nitrogen bridgehead compounds of the general formula I are obtained, wherein R, R^1, R^2, R^3, n and the dotted line are as defined above and R^{10} and R^{11} and R^{12} and R^{13} form a chemical bond, X and Y represent a stripped nitrogen atom, R^6 and R^9 represent an unshared electron-pair, R^5 and R^8 stand for hydrogen or C_{1-4} alkyl, and R^4 and R^7 together form an optionally substituted group of the formula $-(CH_2)_s$ wherein s is 2, 3 or 4.
The reaction may be carried out under the conditions given under item c).

The term "C_{1-4} alkyl" used in the specification includes straight or branched alkyl. The term "optionally substituted C_{6-10} aryl" stands for phenyl or naphthyl, optionally substituted by one or more, same or different substituents selected from C_{1-4} alkyl, C_{1-4} alkoxy, amino, hydroxy, carboxylic acid, carboxylic acid derivative, nitro and halogen. The term "C_{1-4} alkoxy" includes straight and branched alkyl containing alkoxy. The term "carboxylic acid derivative" may stand for alkoxycarbonyl containing C_{1-4} alkoxy, nitrile, amino-carbonyl optionally substituted on the amino group by C_{1-4} alkyl, C_{1-4} acyl, (C_{1-4} dialkyl amino methylene)amino and carbohydrazido. The term "optionally substituted heteroaryl" includes monocyclic or bicyclic compounds containing one or more, same or different heteroatoms, optionally substituted by alkyl, nitro, alkoxy, amino or halogen (such as 2-, 3- or 4-pyridyl, furyl, pyrimidinyl, pyrazinyl, pyridazinyl, etc.).

Heterocyclic compounds of the general formula II used as starting material may be prepared by methods disclosed in Hungarian Patent Specifications Nos.: 156.119, 158.085, 162.384, 162.373 and 166.577 and Dutch Patent Application No. 7 212 286 and the compounds of the general formulae III, IV and V or the compounds used for the preparation thereof are commercially available products.

The salts of the compounds of the general formula I may be alkali salts formed on the carboxy group, such as sodium or potassium salts, ammonium salts, alkali earth metal salts, such as calcium or magnesium salts and salts formed with amines, such as triethylamine.

The new compounds of the general formula I may be used first of all as pharmaceutical intermediate products. The compounds may be converted to pyrido[1,2-a]pyrimidine derivatives substituted in the 9-position by hydrazono group by reacting them with aryl diazonium salts and the obtained end products exhibit pharmaceutical activity, for example anti-allergic activity. Several representatives of the compounds of the general compounds of the formula I themselves show PG-antagonistic, analgetic, anti-artheriosclerotic, tranquillant or other activity.

If the compounds of the general formula I are used in the therapy, then the effective amount of drug supplied daily may vary from 1—1500 mg. administered one or in divides dose(s) depending upon the field of use.

The compounds of the general formula I may be formulated in the form of dragées, tablets, capsules, injections, suspensions, injections, powders, suppositories or other forms and may contain the usual additives, such as disintegrating agents and carriers.

Further details of our invention are illustrated by the following Examples which are given for illustration and not for limitaiton.

EXAMPLE 1

5.9 g. of 3-ethoxy-carbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine and 2.3 ml. of carbon disulfide are dissolved in 35 ml. of ethanol and to the solution of 2.8 g. potassium hydroxide in 25 ml. of ethanol is added dropwise at 25—30°C. The reaction mixture is stirred for 1 hour at room temperature and evaporated at reduced pressure and thus 9.7 g. of 3-ethoxycarbonyl-6-methyl-9-/(bis-thiolate)-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrimidine dipotassium salt are obtained.

EXAMPLE 2

To a solution of 9.7 g. of dipotassium salt of 3-ethoxy-carbonyl-6-methyl-9-//bis-thiolate/-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine (prepared in Example) 1 in 60 ml. of ethanol 4.7 ml. dimethylsulfate is added dropwise under external cooling and the reaction mixture is stirred for 1 hour at 40°C. The precipitated clear yellow crystals are filtered, washed with water and dried. 7.1 g (86%) of 3-ethoxycarbonyl-6-methyl-9-(methyl-thio-thiocarbonyl)-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine are obtained, the product melts at 198—199°C after recrystallization from benzene.

Analysis: for the formula $C_{14}H_{18}N_2O_3S_2$

calculated:	C: 51.51%;	H: 5.56%;	N: 8.58%;
found:	C: 51.70%;	H: 5.78%;	N: 8.48%.

EXAMPLE 3

To 60 ml. ethanol solution of 9.7 g. of dipotassium salt of 3-ethoxycarbonyl-6-methyl-9-//bis-thiolate/-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine prepared according to Example 1 4.7 g. of ethylene bromide are added. The reaction mixture is stirred for 1 hour at 40°C and the precipitated sodium bromide is filtered. The mother liquor is evaporated to half volume and the crystals precipitated upon cooling are filtered and washed with water and dried. 3 g. of 3-ethoxycarbonyl-6-methyl-9-/1,3-dithiolane-2-ylidene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine are obtained, the product melts at 205—207°C after recrystallization from ethanol.

Analysis: for the formula $C_{15}H_{18}N_2O_3S_2$

calculated:	C: 53.23%;	H: 5.36%;	N: 8.27%;
found:	C; 53.17%;	H: 5.41%;	N: 8.22%.

EXAMPLE 4

3.26 g. of 3-ethoxycarbonyl-6-methyl-9-(methyl-thio-thiocarbonyl)-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine are heated in 20 ml. of acetic acid anhydride for 2 hours. The crystals precipitated after cooling are filtered and washed with benzene and dried. 1.6 g. (57.6%) of 3-ethoxy-carbonyl-6-methyl-9-/4-(3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine-9-ylidine/-1,3-dithiethane-2-ylidene)-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine is obtained which melts at 315—318°C after recrystallization from dimethylformamide.

Analysis: for the formula $C_{26}H_{28}N_4O_6S_2$

calculated:	C: 56.10%	H: 5.07%;	N: 10.07%;	S: 11.52%;
found:	C: 55.89%;	H: 4.98%	N: 10.20%;	S: 10.80%.

EXAMPLE 5

To a mixture of 16.3 g. of phosgene-N,N-dimethyl-immonium-chloride in 50 ml. dichloromethane 23.6 g. of 3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine in 30 ml. of dichloromethane is added dropwise under stirring and the reaction mixture is heated for 3 hours. When the solvent is distilled off the residual substance is crystallized with ether.

35.2 g. of highly hygroscopic 3-ethoxycarbonyl-6-methyl-9-/(chloro-N,N-dimethylammonio)-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride is obtained and dried *in vacuo*.

Analysis for the formula $C_{15}H_{20}N_3O_3Cl_2$

calculated: Cl_{ionic}: 19.6%; found: Cl_{ionic}: 19.4%.

EXAMPLE 6

A solution of 1.8 g. of 3-ethoxycarbonyl-6-methyl-9-/(chloro-N,N-dimethylammonio)-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride and 5 mmoles of sodium acetate in 5 ml. of anhydrous ethanol is allowed to stand for 24 hours at room temperature and the precipitated sodium chloride is filtered and the filtrate is evaporated. The residue is dissolved in water and the pH of the solution is adjusted to 7 by adding sodium hydrogen carbonate. The precipitated crystals are filtered, washed with water and dried. 0.92 g. (60%) of 3,9-diethoxycarbonyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine is obtained, melting point: 138—140°C.

Analysis: for the formula $C_{15}H_{20}N_2O_5$

calculated:	C: 58.43%;	H: 6.54%;	N: 9.09%;
found:	C: 58.65%;	H: 6.54%;	N: 9.06%.

EXAMPLE 7

A solution of 1.8 g. of 3-ethoxycarbonyl-6-methyl-9-/(chloro-N,N-dimethyl-ammonio)-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride and 5 mmoles of sodium acetate in 5 ml. of anhydrous methanol is allowed to stand for 24 hours at room temperature and the precipitated sodium chloride is filtered and the filtrate is evaporated. The residue is dissolved in water and the pH of the solution is adjusted to 7 by adding sodium carbonate. The precipitated crystals are filtered and washed with water and dried.

0.96 g. (65%) of 3-ethoxycarbonyl-6-methyl-9-methoxy-carbonyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine is obtained which melts at 136—139°C.

Analysis: for the formula $C_{14}H_{18}N_2O_5$

calculated:	C: 57.14%;	H: 6.17%;	N: 9.52%;
found:	C: 57.00%;	H: 6.25%;	N: 9.52%.

EXAMPLES 8 TO 13

To a solution of 3.65 g. of 3-ethoxycarbonyl-6-methyl-9-/(chloro-N,N-dimethyl-ammonio)-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride in 15 ml. of anhydrous dichloromethane 0.02 mole of amine is added and the reaction mixture is stirred for 1 hour. After cooling the precipitated amine hydrochloride is filtered. The filtrate is evaporated. The oily, crystallizing residue is crystallized with ether. The obtained crystals are filtered, washed with ether and dried. The product is recrystallized from anhydrous ethanol. The obtained substances and date thereof are shown in Table 1.

TABLE 1

Example No.	Amine	Product	Yield %	Mp. °C	Empirical formula	Analysis calculated found C%	H%	N%
8	aniline	3-ethoxycarbonyl-6-methyl-9-(N-phenyl-N′,N′-dimethyl-formamidinium)-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]-pyrimidine-chloride	74	236–239 (decomp.)	$C_{21}H_{27}N_4O_3Cl$	60.30	6.45	13.40
						60.08	6.54	13.42
9	4-chloroaniline	3-ethoxycarbonyl-6-methyl-9-/N-(4-chloro-phenyl)-N′,N′-dimethyl-formamidinium/-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride	75	230–232 (decomp.)	$C_{21}H_{26}N_4O_3Cl_2$	55.60	5.74	12.35
						54.95	5.73	12.26
10	4-methylaniline	3-ethoxycarbonyl-6-methyl-9-/N-(4-methyl-phenyl)-N′,N′-dimethyl-formamidinium/-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride	81	225–226 (decomp.)	$C_{22}H_{29}N_4O_3Cl$	61.10	6.70	12.92
						60.83	6.81	12.79
11	4-methoxyaniline	3-ethoxycarbonyl-6-methyl-9-/N-(4-methoxy-phenyl)-N′,N′-dimethyl-formamidinium/-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride	38	222–224 (decomp.)	$C_{22}H_{29}N_4O_4Cl$	58.95	6.47	12.50
						58.58	6.65	12.58
12	2-naphthylamine	3-ethoxycarbonyl-6-methyl-9-/N-(2-naphthyl)-N′,N′-dimethyl-formamidinium/-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride	68	234–235	$C_{25}H_{29}N_4O_3Cl$	64.10	6.19	11.95
						63.69	6.17	11.82
13	2-methoxy-carbonyl-aniline	3-ethoxycarbonyl-6-methyl-9-/N-(2-methoxy-carbonyl-phenyl)-N′,N′-dimethyl-formamidinium/-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride	63	210–211 (decomp.)	$C_{23}H_{29}N_4O_5Cl$	57.91	6.09	11.75
						57.33	6.09	11.76

EXAMPLE 14

To an aqueous solution of 4.2 g. of 3-ethoxycarbonyl-6-methyl-9-(N-phenyl-N',N'-dimethyl-formamidinium)-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride a 20 by % W/V solution of potassium carbonate is added. The precipitated crystals are filtered, washed with water and dried.

3.4 g. (89%) of 3-ethoxycarbonyl-6-methyl-9-(N-phenyl-N',N'-dimethyl-formamidino)-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine is obtained which after recrystallization from ethanol melts at 193—195°C.

Analysis: for the formula $C_{21}H_{26}N_4O_3$

calculated:	C: 65.98%;	H: 6.81%;	N: 14.65%;
found:	C: 65.89%;	H: 6.79%;	N: 14.69%.

EXAMPLE 15

To a mixture of 22.1 g. of phosgene-N-methyl-N-phenyl-immonium chloride in 50 ml. of dichloromethane 23.6 g. of 3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine in 30 ml. of dichloromethane is added dropwise and the reaction mixture is boiled for 3 hours. The solvent is distilled off and the residue is crystallized with ether.

41.2 g of highly hygroscopic 3-ethoxycarbonyl-6-methyl-9-/(chloro-N-methyl-N-phenyl-ammonio)-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride is obtained and dried in vacuo.

Analysis: for the formula $C_{20}H_{23}N_3O_3Cl_2$

calculated: Cl_{ionic}: 8.36%; found: Cl_{ionic}: 8.45%.

EXAMPLE 16

To a solution of 21 g. of 3-ethoxycarbonyl-6-methyl-9-/(chloro-N-methyl-N-phenyl-ammonio)-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride in 20 ml. of anhydrous dichloromethane 0.2 mole of aniline is added and the reaction mixture is boiled for 1 hour. After cooling the precipitated aniline hydrochloride is filtered. The dichloromethane mother liquor is evaporated. The residue is crystallized from ether. The precipitated crystals are filtered, washed with ether and dried.

25.9 g. (54%) of 3-ethoxycarbonyl-6-methyl-9-(N',N'-diphenyl-N-methyl-formamidinium)-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride is obtained, which melts at 186—188°C under decomposition after recrystallization from ethanol.

Analysis: for the formula $C_{26}H_{29}N_4O_3Cl$

calculated:	C: 64.95%;	H: 6.04%;	N: 11.66%;
found:	C: 64.76%;	H: 6.09%;	N: 11.26%.

EXAMPLE 17

To an aqueous solution of 24 g. of 3-ethoxycarbonyl-6-methyl-9-(N,N'-diphenyl-N-methyl-formamidinium)-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride a 20% by W/V solution of potassium carbonate is added dropwise. The precipitated crystals are filtered and washed with water and dried. 16.7 g. (75%) of 3-ethoxycarbonyl-6-methyl-9-(N,N'-diphenyl-N-methyl-formamidino)-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine is obtained, which after recrystallization from ethanol melts at 199—202°C.

Analysis: for the formula $C_{26}H_{28}N_4O_3$

calculated:	C: 70.25%;	H: 6.31%;	N: 12.61%;
found:	C: 69.97%;	H: 6.27%;	N: 12.42%.

EXAMPLE 18

To a solution of 21 g. of 3-ethoxycarbonyl-6-methyl-9-/(chloro-N-methyl-N-phenyl-ammonio)-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride in 20 ml. of anhydrous dichloromethane 0.2 mole of 4-chloro-aniline is added and the reaction mixture is boiled for 1 hour. The 4-chloro-aniline-hydrochloride precipitated after cooling is filtered. The dichloromethane mother liquor is evaporated. The obtained 3-ethoxycarbonyl-6-methyl-9-/N-(4-chloro-phenyl)-N'-methyl-formamidinium/-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride is dissolved in water and to the solution a 20% by W/V solution of potassium carbonate is added. The precipitated crystals are filtered, washed with water and dried. 13.3 g. (55.5%) of 3-ethoxycarbonyl-6-methyl-9-/N-(4-chloro-phenyl)-N'-phenyl-N'-methyl-formamidino/-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine is obtained, which melts at 194—196°C after recrystallization from ethanol.

Analysis: for the formula $C_{26}H_{27}N_4O_3Cl$

calculated:	C: 65.15%;	H: 5.65%;	N: 11.71%;
found:	C: 64.85%;	H: 5.83%;	N: 11.66%.

EXAMPLE 19

To 21 g. of 3-ethoxycarbonyl-6-methyl-9-/(chloro-N-methyl-N-phenyl-ammonio)-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride dissolved in 20 ml. of anhydrous dichloromethane 0.2 mole of 4-methyl-aniline is added and the reaction mixture is stirred for 1 hour.

After cooling the precipitated 4-methyl-aniline-hydrochloride is filtered. The dichloromethane filtrate is evaporated. The obtained 3-ethoxy-carbonyl-6-methyl-9-/N'-(4-methyl-phenyl)-N'-phenyl-N'-methyl-formamidinium/-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride is dissolved in water. To the aqueous solution 20% by W/V solution of potassium carbonate is added. The precipitated crystals are filtered, washed with water and dried.

14.7 g. (64%) of 3-ethoxycarbonyl-6-methyl-9-/N'-(4-methyl-phenyl)-N'-phenyl-N'-methyl-formamidino/-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine is obtained, which after recrystallization from ethanol melts at 161—163°C.

Analysis: for the formula $C_{27}H_{30}N_4O_3$

calculated:	C: 70.75%;	H: 6.56%;	N: 12.21%;
found:	C: 70.35%;	H: 6.62%;	N: 11.91%.

EXAMPLES 20 TO 23

To a dichloromethane solution of 0.05 mole of a nitrogen bridgehead compound 0.055 mole of isocyanate is added dropwise at room temperature and the reaction mixture is heated for 10 hours and allowed to stand for 2 days, whereafter the solvent is distilled off. The residue is crystallized from ethanol. The prepared products are shown in Table 2.

TABLE 2

Example No.	Starting material	Isocyanate	Product	Yield %	Mp. °C	Empirical formula	Analysis calculated found C%	H%	N%
20	3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetra-hydro-4H-pyrido-[1,2-a]pyrimidine	phenyl-isocyanate	3-ethoxycarbonyl-6-methyl-9-/N-phenyl-amino-carbonyl/-4-oxo-1,6,7,8-tetra-hydro-4H-pyrido-[1,2-a]pyrimidine	46	200–201	$C_{19}H_{21}N_3O_4$	64.21 63.95	5.95 5.81	11.83 11.65
21	3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetra-hydro-4H-pyrido-[1,2-a]pyrimidine	chloro-acetyl-isocyanate	3-ethoxycarbonyl-6-methyl-9-)chloro-acetyl-amino-carbonyl)-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine	74	158–160	$C_{15}H_{18}N_3O_5Cl$	50.63 51.02	5.06 5.02	11.80 11.63
22	3-ethoxycarbonyl 6-methyl-4-oxo 6.7.8.9-tetra-hydro-4H-pyrido-[1,2-a]pyrimidine	tozyl-isocyanate	3-ethoxycarbonyl-6-methyl-9-(toxyl-amino-carbonyl)-4-oxo-1,6,7,8-tetra-hydro-4H-pyrido-[1,2-a]pyrimidine	80	182–183	$C_{20}H_{23}N_3O_6S$	55.42 55.92	5.35 5.30	9.69 9.72
23	3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetra-hydro-4H-pyrido-[1,2-a]pyrimidine	tozyl-isocyanate	3-/(tozylamino-carbonyl)-aminocarbonyl/-6-methyl-9-(tozyl-amino-carbonyl)-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine	49	164	$C_{26}H_{27}N_5O_8S_2$	51.90 52.28	4.52 4.48	11.64 11.51

EXAMPLES 24 TO 28

A mixture of 23.6 g. of 3-ethoxycarbonyl-6-methyl-4-oxo-4H-pyrido[1,2-a]pyrimidine and 0.1 mole of isocyanate is stirred for 72 hours at 40—50°C. The formed thick viscous reaction mixture is suspended in 200 ml. of ethanol, filtered and washed with ethanol (when using n-butyl-isocyanate the reaction is carried out at 80—100°C). The prepared compounds are shown in Table 3.

TABLE 3

Example No.	Isocyanate	Product	Yield %	Mp. °C	Empirical formula	Analysis calculated found C%	H%	N%
24	n-butyl-isocyanate	3-ethoxycarbonyl-6-methyl-9-/(n-butylamino)-carbonyl/-4-oxo-1,6-7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine	35	152–155	$C_{17}H_{25}N_3O_4$	60.90 60.25	7.47 7.41	12.52 12.40
25	phenyl-isocyanate	3-ethoxycarbonyl-6-methyl-9-/(phenyl-amino)-carbonyl/-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine	74	198–200	$C_{19}H_{21}N_3O_4$	No melting point depression with the product of Example 20		
26	4-chloro-phenyl-isocyanate	3-ethoxycarbonyl-6-methyl-9-/(4-chloro-phenyl-amino)-carbonyl/-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]-pyrimidine	82	206–210	$C_{19}H_{20}N_3O_4Cl$	58.50 58.10	5.13 5.07	10.78 10.59
27	3-chloro-phenyl-isocyanate	3-ethoxycarbonyl-6-methyl-9-/(3-chloro-phenyl-amino/-carbonyl/-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]-pyrimidine	78	194–198	$C_{19}H_{20}N_3O_4Cl$	58.50 58.21	5.13 5.05	10.78 10.61
28	3,4-dichloro-phenyl-isocyanate	3-ethoxycarbonyl-6-methyl-9-/(3,4-dichloro-phenyl-amino)-carbonyl/-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine	79	208–212	$C_{19}H_{19}N_3O_4Cl_2$	53.80 53.28	4.48 4.40	9.90 9.78

EXAMPLE 29

A solution of 1.8 g. of 3-ethoxycarbonyl-6-methyl-9-/(chloro-N,N-dimethyl-ammonio)-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride in 5 ml. of ethanol is boiled for 30 minutes. The crystals are precipitated after cooling, filtered, washed with ethanol and dried.

1.08 g. (63%) of 3-ethoxycarbonyl-6-methyl-9-(N,N-dimethylamino-carbonyl)-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine hydrochloride is obtained, which after recrystallization from ethanol melts at 166—168°C (decomposition).

Analysis: for the formula $C_{15}H_{22}N_3O_4Cl$

calculated:	C: 52.40%;	H: 6.45%;	N: 12.22%;	Cl: 10.31%;
found:	C: 52.18%;	H: 6.58%;	N: 12.30%;	Cl: 10.45%.

EXAMPLE 30

3.26 g. of 3-ethoxycarbonyl-6-methyl-9-(methylthio-thiocarbonyl)-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]-pyrimidine and 0.6 g. of ethylene diamine are boiled in 50 ml. of benzene for 10 hours. The precipitated yellow crystals are filtered, covered with benzene and dried.

1.9 g. (62%) of 3-ethoxycarbonyl-6-methyl-9-(2-imidazolidene)-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine are obtained, which melts at 252—254°C after recrystallization from dimethylformamidine.

Analysis: for the formula $C_{15}H_{18}N_4O_3$

calculated:	C: 59.15%;	H: 5.90%;	N: 18.40;
found:	C: 58.91%;	H: 5.85%;	N: 18.35%.

EXAMPLE 31

1.0 g. of 3-ethoxycarbonyl-6-methyl-9-(2-imidazolidene)-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine is dissolved in 10 ml. of ethanol and the solution is saturated with hydrogenchloride gas and evaporated. The residue is recrystallized from a mixture of ethanol and ether.

0.9 g. of 3-ethoxycarbonyl-6-methyl-9-(2-imidazolidene)-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine-bis hydrochloride is obtained, melting under decomposition at 190°C.

Analysis: for the formula $C_{15}H_{20}N_4O_3Cl_2$

calculated:	C: 48.01%;	H: 5.37%;	N: 14.93%;	Cl: 18.90%;
found:	C: 47.82%;	H: 5.18%;	N: 15.06%;	Cl 19.01%.

EXAMPLE 32

3.6 g. of 3-ethoxycarbonyl-6-methyl-9-/(chloro-N,N-dimethylammonio)-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride are stirred with 1.2 g. of ethylenediamine in 40 ml. of dimethylformamide at 40°C for 2 hours and after cooling the precipitated crystals are filtered, washed with water and dried.

1.0 g. of 3-ethoxycarbonyl-6-methyl-9-(2-imidazolidene)-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine is obtained, which melts at 252—254°C.

EXAMPLE 33

A mixture of 2.0 g. of 3-amino-carbonyl-2,6-dimethyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine and 2.2 g. of phenyl isocyanate is heated to 80°C and the obtained solution is stirred for 10 hours at 40—60°C. After cooling the reaction mixture is treated with ether and the precipitated crystals are filtered, washed with ether and dried. The obtained crystals are dissolved in ethanol, filtered and the filtrated is placed to a refrigerator and allowed to crystallize. The precipitated crystals are filtered, washed with ethanol.

1.4 g. of 3-amino-carbonyl-9-(phenylamino-carbonyl)-2,6-dimethyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine is obtained, melting point: 187—188°C.

Analysis: for the formula $C_{18}H_{20}N_4O_3$

calculated:	C: 63.51%;	H: 5.92%;	N: 16.46%;
found:	C: 63.49%;	H: 6.00%;	N: 16.26%.

EXAMPLE 34

1.6 g. of potassium hydroxide is dissolved in 20 ml. of ethanol. To this solution 3.6 g. 3-ethoxycarbonyl-9-(phenylamino-carbonyl)-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine dissolved in ethanol is added. The reaction mixture is boiled for 30 minutes and the crystals precipitated after cooling are filtered, washed with chloroform and dried.

3.1 g. of potassium salt of 9-(phenylamino-carbonyl)-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine-3-carboxylate is obtained which is decomposed at 276—280°C.

Analysis: for the formula $C_{17}H_{16}N_3O_4K$

calculated:	C: 55.88%;	H: 4.41%;	N: 11.50%;
found:	C: 56.02%;	H: 4.50%;	N: 11.42%.

EXAMPLE 35

3.1 g. of potassium salt of 9-(phenyl-amino-carbonyl)-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine-3-carboxylate are dissolved in 250 ml. of water under heating. The pH of the solution is adjusted to 1 at 40—50°C by adding an about 38% by W/V solution of hydrochloric acid. The crystals precipitated upon cooling are filtered, washed with water and dried. The obtained 2.2 g. of product is crystallized from acetonitrile.

Thus 9-(phenyl-amino-carbonyl)-3-carboxy-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine is obtained, melting point: 200—201°C. Yield: 25%.

Analysis: for the formula $C_{17}H_{17}N_3O_4$

calculated: C: 62.37%; H: 5.24%; N: 12.84%;
found: C: 62.18%; H: 5.18%; N: 12.45%.

EXAMPLE 36

2 g. of 6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine are reacted with phosgene-N,N-dimethyl-immonium chloride as described in Example 5. Thus highly hygroscopic 6-methyl-9-/(chloro-N,N-dimethyl-ammonio)-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride is obtained, which is dried in vacuo.

Analysis: for the formula $C_{12}H_{17}N_3OCl_2$

calculated: Cl_{ionic}: 12.22%; found: Cl_{ionic}: 12.10%.

EXAMPLE 37

6-Methyl-9-/(chloro-N,N-dimethylammonio)-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride is boiled for 30 minutes in ethanol. The reaction mixture is evaporated and the obtained 6-methyl-9-(N,N-dimethylamino-carbonyl)-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine hydrochloride is converted to base by conventional methods. The base is crystallized from petrolether.

Thus 6-methyl-9-(N,N-dimethylamino-carbonyl)-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine is obtained, melting point: 78°C.

Analysis: for the formula $C_{12}H_{17}N_3O_2$

calculated: C: 61.26%; H: 7.28%; N: 17.86%;
found: C: 61.40%; H: 7.11%; N: 17.69%.

EXAMPLE 38

3-Cyano-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine is reacted as described in Example 5 with phosgene-N,N-dimethyl-immonium chloride.

Thus highly hygroscopic 3-cyano-6-methyl-9-/(chloro-N,N-dimethyl-ammonio)-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride is obtained.

Analysis: for the formula $C_{13}H_{16}N_4OCl_2$

calculated: Cl_{ionic}: 10.70%; found: Cl_{ionic}! 10.52%.

EXAMPLE 39

3-Cyano-6-methyl-9-/(chloro-N,N-dimethyl-ammonio)-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine chloride is treated as given in Example 29. The ethanol solution is evaporated and the obtained residue is crystallized from ethyl acetate.

Thus 3-cyano-6-methyl-9-(N,N-dimethylamino-carbonyl)-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine is obtained, yield: 60%.

Analysis: for the formula $C_{13}H_{16}N_4O_2$

calculated: C: 59.98%; H: 6.20%; N: 21.51%;
found: C: 59.90%; H: 6.11%; N: 21.22%.

EXAMPLE 40

3.4 g. of 3-ethoxycarbonyl-6-methyl-9-(N,N-dimethyl-amino-carbonyl)-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine hydrochloride are dissolved in 20 ml. of water and the solution is neutralized with a 5% by W/V solution of sodium hydrogen carbonate. The reaction mixture is shaken out with chloroform. The chloroform solution is dried above sodium sulfate, filtered and evaporated. The residue is crystallized from a mixture of ethanol and water.

2.1 g. of 3-ethoxycarbonyl-6-methyl-9-(N,N-dimethyl-amino-carbonyl)-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine is obtained.

Analysis: for the formula $C_{15}H_{21}N_3O_4$

calculated: C: 58.60%; H: 6.90%; N: 13.66%;
found: C: 58.25%; H: 6.94%; N: 13.56%.

EXAMPLE 41

3.07 g. of 3-ethoxycarbonyl-6-methyl-9-(N,N-dimethyl-amino-carbonyl)-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine are dissolved in ethanol. To the solution a 20% by W/V solution

of ammonia in ethanol is added and the reaction mixture is allowed to stand in a closed vessel at room temperature for 3 days. The precipitated crystals are filtered, washed with ethanol.

1.18 g. of 3-aminocarbonyl-6-methyl-9-(N,N-dimethyl-amino-carbonyl)-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine is obtained, melting point 220°C.

Analysis: for the formula $C_{13}H_{18}N_4O_3$

calculated:	C: 56.09%;	H: 6.53%;	N: 20.12%;
found:	C: 55.89%;	H: 6.52%;	N: 20.33%.

EXAMPLE 42

3,6-Diethoxycarbonyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine is treated with ethanolic ammonia as disclosed in Example 41.

1.51 g. of 3-aminocarbonyl-9-ethoxycarbonyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine is obtained, melting point: 251°C.

Analysis: for the formula $C_{13}H_{17}N_3O_4$

calculated:	C: 57.12%;	H: 6.28%;	N: 15.30%;
found:	C: 56.98%;	H: 6.12%;	N: 15.50%.

EXAMPLE 43

0.416 g. of 3-ethoxycarbonyl-4-oxo-4,6,7,8-tetrahydro-pyrrolo[1,2-a]pyrimidine is dissolved in 4 ml. of benzene and to the solution 0.24 g. of phenyl-isocyanate is added. The reaction mixture is allowed to stand for 5 days at room temperature and the precipitated crystals are filtered and washed with benzene.

0.50 g. (76.5%) of 3-ethoxycarbonyl-8-(N-phenyl-amino-carbonyl)-4-oxo-1,4,6,7-tetrahydro-pyrrolo[1,2-a]pyrimidine is obtained, melting point: 240—241°C.

Analysis: for the formula $C_{17}H_{17}N_3O_4$

calculated:	C; 62.38%;	H: 5.23%;	N: 12.84%;
found:	C: 62.51%;	H: 5.15%;	N: 12.90%.

EXAMPLE 44

0.8 g. of 3-cyano-4-oxo-4,6,7,8-tetrahydro-pyrrolo[1,2-a]pyrimidine and 0.6 ml. of carbon disulfide are dissolved in 10 ml. of ethanol and to the solution 0.6 g. of potassium hydroxide in 10 ml. of ethanol is added dropwise. The reaction mixture is stirred for 1 hour at room temperature and evaporated at reduced pressure.

Thus 3-cyano-9-/(bis-thiolate)-methylene/-4-oxo-4,6,7,8-tetrahydro-pyrrolo[1,2-a]pyrimidine dipotassium salt is obtained.

EXAMPLE 45

3-Cyano-9-/(bis-thiolat)-methylene/-4-oxo-4,6,7,8-tetrahydro-pyrrolo[1,2-a]pyrimidine dipotassium salt as prepared according to Example 44 is dissolved in 20 ml. of ethanol and to the solution 1.25 g. dimethylsulfate is added and the reaction mixture is stirred for 1 hour at 40°C. The precipitated crystals are filtered, washed with ethanol.

0.46 g. (36.5%) of 3-cyano-9-(methylthio-thiocarbonyl)-4-oxo-1,4,6,7-tetrahydro-pyrrolo[1,2-a]pyrimidine is obtained, which melts at 202—3°C.

Analysis: for the formula $C_{10}H_9N_3OS_2$

calculated:	C: 47.79%;	H: 3.61%;	N: 16.72%:
found:	C: 48.01%;	H: 3.52%;	N: 16.81%.

EXAMPLE 46

To 0.66 g. of an oily 80% sodium hydride suspension 50 ml. of benzene are added, whereafter 4.72 g. of 3-ethoxy-carbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine dissolved in 15 ml. of benzene are added dropwise. After stirring for 30 minutes a solution of 2.96 g. of methyl thioisocyanate in 10 ml. of benzene is added within 10 minutes at a temperature of 25 to 35°C. The mixture is stirred for 2 hours and by adding 80 ml. of ether the sodium salt of the formed 3-ethoxycarbonyl-6-methyl-9-(methylamino-thiocarbonyl)-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine is precipitated in an oily form. The solvent is discarded and the residue is triturated with ether and dried in a vacuum desiccator. Thus 5.3 g. (80%) of the amorphous 3-ethoxycarbonyl-6-methyl-9-(methylamino-thiocarbonyl)-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine are obtained in the form of a sodium salt.

EXAMPLE 47

To the sodium salt of the 3-ethoxycarbonyl-6-methyl-9-(methylamino-thiocarbonyl)-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine obtained by the process of Example 46, 15 ml. of acetone and 130 ml. of water are added, the pH value of the solution is thereafter adjusted to 3—4 by the addition of acetic acid. The precipitated crystals are filtered, washed with water and dried, recrystallized from ethyl alcohol. Thus 3.2 g. of the 3-ethoxycarbonyl-6-methyl-9-(methylamino-

thiocarbonyl)-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine are obtained, melting at 199 to 200°C. Yield: 52%.

Analysis based on the formula $C_{14}H_{19}N_3O_3S$:

calculated:	C: 54.35%;	H: 6.19%;	N: 13.58%;
found:	C: 54.45%;	H. 6.18%;	N: 13.72%.

EXAMPLE 48

To 0.66 g. of an oily 80% sodium hydride suspension 50 ml. of benzene are added, whereafter 4.72 g. of 3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine dissolved in 15 ml. of benzene are added dropwise. After stirring for 30 minutes 5.4 g. of phenyl thioisocyanate dissolved in 10 ml. of benzene is added within 10 minutes at a temperature of 25—35°C. The mixture is stirred for 2 hours and by adding 80 ml. of ether the sodium salt of the formed 3-ethoxycarbonyl-6-methyl-9-(phenylamino-thiocarbonyl)-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine is precipitated in an oily form. The solvent is discarded and the residue is triturated with ether and the product is dried in a vacuum desiccator. Thus 6.1 g. (76%) of the amorphous sodium salt of the 3-ethoxycarbonyl-6-methyl-9-(phenylamino-thiocarbonyl)-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine are obtained.

EXAMPLE 49

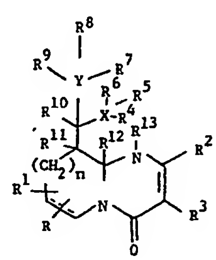
To the sodium salt of the 3-ethoxycarbonyl-6-methyl-9-(phenylamino-thiocarboinyl)-4-oxo-6,7,8,9-tetrahydro-4H-pyrido[1,2-a]pyrimidine obtained according to the process of Example 48, 15 ml. of acetone and 130 ml. of water are added, whereafter the pH value of the solution obtained is adjusted to 3—4 by the addition of acetic acid. The precipitated crystals are filtered, washed with water and dried, recrystallized from acetonitrile. Thus 3.2 g. (52%) of the 3-ethoxycarbonyl-6-methyl-9-(phenylamino-thiocarbonyl)-4-oxo-1,6,7,8-tetrahydro-4H-pyrido[1,2-a]pyrimidine are obtained, melting at 173—175°C.

Analysis based on the formula $C_{18}H_{21}N_3O_3S$:

calculated:	C: 61.44%;	H: 5.70%;	N: 11.31%;
found:	C: 61.75%;	H: 5.57%;	N: 11.40%.

CLAIMS

1. Compounds of the general formula



I

[wherein

R represents hydrogen or C_{1-4} alkyl,

R^1 represents hydrogen or C_{1-4} alkyl and

R and R^1 together may form a —(CH=CH$)_2$ group being attached to the two adjacent ring carbon atoms and the dotted line represents a carbon-carbon bond,

R^2 represents hydrogen, C_{1-4} alkyl,

R^3 represents hydrogen, C_{1-4} alkyl, phenyl, carboxy or salt thereof, alkoxycarbonyl containing 1—6 carbon atoms in alkoxy moiety, carbamoyl, cyano, —CO—NH—CO—SO_2—C_6H_4—*p*—CH_3 or —$(CH_2)_s$—$COOR^{14}$ (wherein s is 1, 2 or 3 and R^{14} represents hydrogen or C_{1-4} alkyl,

n represents 0 or 1,

(a) if R^{13} represents hydrogen and R^{12} and R^{11} and R^9 and R^{10} together each form a chemical bond then Y represents an oxygen or sulfur atom without their lone pairs of electrons in which case R^7 and R^8 each represent a lone pair of electrons; or

Y represents a nitrogen atom without its lone pair of electrons,

R^7 represents C_{1-4} alkyl, optionally substituted C_{6-10} aryl or C_{7-12} aralkyl,

R^8 represents a lone pair of electrons or C_{1-4} alkyl and in this latter case a salt is formed with the positive nitrogen atom; and

X, R^4, R^5, R^6 together represent halogen; or

X represents an oxygen or sulfur atom without their lone pairs of electrons,

R^4 represents hydrogen or C_{1-4} alkyl,

R^5 and R^6 each represent an unshared lone pair of electrons; or

X represents a nitrogen atom without its lone pair of electrons and

R^4 represents chloroacetyl, C_{1-4} alkyl, optionally substituted C_{6-10} aryl or optionally substituted heteroaryl,

R^5 represents hydrogen or alkyl and R^6 represents a lone pair of electrons; or

(b) if R^{12} and R^{13} together form a chemical bond, R^{11} represents hydrogen and R^9 and R^{10} together form a chemical bond, then

R^4, R^5, R^6, R^7, R^8, X and Y are as defined in item (a) and

(c) if R^{10} and R^{11} and R^{12} and R^{13} together each form a chemical bond, then

Y represents an oxygen or sulfur atom without its lone pairs of electrons and if R^7, R^8 and R^9 each represent an unshared lone pair of electrons, then a positive cation forms a salt with the thus formed anion, or

R^8 and R^9 each represent an unshared lone pair of electrons, and

R^7 represents hydrogen or C_{1-4} alkyl; or

Y represents a nitrogen atom without its lone pair of electrons,

R^7 represents hydrogen, C_{1-4} alkyl or optionally substituted C_{6-10} aryl

R^8 is C_{1-4} alkyl, and

R^9 represents a lone pair of electrons; and

X, R^5, R^6, R^7 together represent halogen; or

X represents an oxygen or sulfur atom without their lone pairs of electrons and if R^4, R^5 and R^6 represent a lone pair of electrons, then a positive cation forms a salt with the thus formed anion, or

R^4 represents hydrogen or C_{1-4} alkyl, and

R^5 and R^6 each represent an unshared lone pair of electrons; or

X represents a nitrogen atom without its lone pair of electrons and

R^4 represents chloroacetyl, C_{1-4} alkyl, optionally substituted C_{6-10} aryl or optionally substituted heteroaryl,

R^5 represents hydrogen or C_{1-4} alkyl, and

R^6 represents an unshared lone pair of electrons;

and if Y and X each represent an oxygen or sulfur atom without their lone pairs of electrons and R^5, R^6, R^7, R^8 and R^9 each represent a lone pair of electrons or if

Y and X each represent a nitrogen atom without its lone pair of electrons and R^6 and R^9 each represent a lone pair of electrons, R^5 and R^8 each represent hydrogen or C_{1-4} alkyl, then

R^4 and R^7 together form an optionally substituted $-(CH_2)_s-$ group (wherein s is 1, 2, 3 or 4)] and the tautomers and salts thereof.

2. Compounds as claimed in claim 1, wherein n is 1.

3. Compounds as claimed in claim 1, wherein R represents hydrogen.

4. Compounds as claimed in claim 1 wherein R^1 represents hydrogen.

5. Compounds as claimed in any one of claims 1 to 3 wherein R^1 represents C_{1-4} alkyl.

6. Compounds as claimed in claim 5 wherein R^1 represents methyl.

7. Compounds as claimed in any one of claims 1 to 6 wherein R^3 represents an alkali metal salt of a carboxy group.

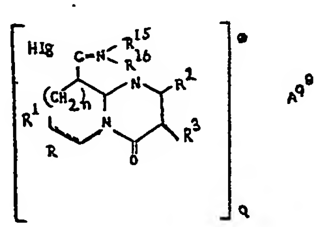
8. Compounds as claimed in any one of Claims 1 to 6 wherein R^3 represents carboxy, methoxycarbonyl, ethoxycarbonyl or carbamoyl.

9. Compounds as claimed in any one of the preceding claims in the form of the physiologically compatible salts thereof.

10. Compounds as claimed in any one of the preceding claims in the form of an optically active isomer thereof.

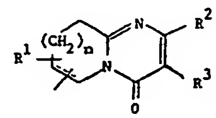
11. Compounds as claimed in claim 1 as herein specifically disclosed.

12. A process for the preparation of compounds as claimed in claim 1 having the formula



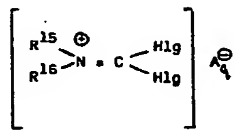
Ia

(wherein R, R^1, R^2, R^3 and n are as defined in claim 1, Hlg represents halogen, R^{15} represents C_{1-4} alkyl or optionally substituted C_{6-10} aryl, R^{16} represents C_{1-4} alkyl, A represents an anion and q represents the charge on the anion) or a tautomer thereof which process comprises reacting a compound of the formula



II

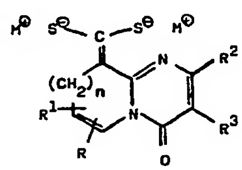
(wherein R, R^1, R^2, R^3, n and the dotted line are as defined in claim 1) or a tautomer thereof with a compound of the general formula



III

(wherein Hlg represents halogen, R^{15} represents C_{1-4} alkyl or optionally substituted C_{6-10} aryl, R^{16} represents C_{1-4} alkyl, A represents an anion and q represents the charge on the anion) whereby a compound of formula Ia as hereinbefore defined or a tautomer thereof is obtained.

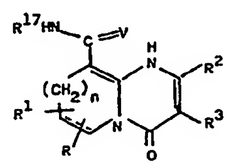
13. A process for the preparation of compounds as claimed in claim 1 having the formula



Ib

(wherein R, R^1, R^2, R^3, n, Hlg and the dotted line are as defined in claim 1 and M represents a cation) or a tautomer thereof, which process comprises reacting a compound of formula II (as defined in claim 12) or a tautomer thereof with carbon disulfide whereby a compound of formula Ib as herein defined or a tautomer thereof is obtained.

14. A process for the preparation of compounds as claimed in claim 1 having the formula



Ic

(wherein R, R^1, R^2, R^3, n and the dotted line are as defined in claim 1, R^{17} represents C_{1-4} chloroacetyl, substituted C_{6-10} aryl or optionally substituted C_{6-10} aryl or optionally substituted heteroaryl and V represents an oxygen or sulfur atom) or a tautomer thereof, which process comprises reacting a compound of formula II as defined in claim 12 or a tautomer thereof with an isocyanate of the general formula

$$R^{17}—N=C=V \qquad V$$

wherein R^{17} represents C_{1-4} alkyl, chloroacetyl, optionally substituted C_{6-10} aryl or optionally substituted heteroaryl, V stands for an oxygen or sulfur atom wherein a compound of formula Ic as herein defined or a tautomer thereof is obtained.

15. A process for the preparation of compounds as claimed in claim 1 (wherein R, R^1, R^2, R^3, n and the dotted line are as defined in claim 1, R^9 and R^{10} together and R^{11} and R^{12} together each form a chemical bond, R^{13} represents hydrogen, X and Y represent sulfur, R^5, R^6, R^7 and R^8 each represent an unshared lone pair of electrons and R^4 represents C_{1-4} alkyl) or a tautomer thereof, which process comprises alkylating a compound of the general formula I (wherein R, R^1, R^2, R^3, n and the dotted line are as defined in claim 1, R^{10} and R^{11} together and R^{12} and R^{13} together each form a chemical bond, X and Y each represent sulfur and R^4, R^5, R^6, R^7, R^8 and R^9 each represent an unshared lone pair of electrons, a salt being formed between the dianion and a cation) or a tautomer thereof whereby the said compound as claimed in claim 1 is obtained.

16. A process as claimed in claim 15 wherein the said cation is an alkali metal cation.

17. A process for the preparation of compounds as claimed in claim 1 [wherein R, R^1, R^2, R^3, n and the dotted line are as defined in claim 1, R^{10} and R^{11} together and R^{12} and R^{13} together each form a

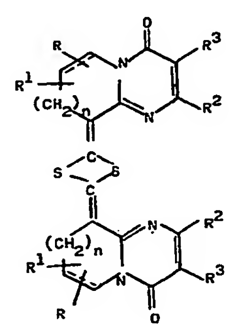
chemical bond, X and Y each represent sulfur and R^5, R^6, R^8 and R^9 each represent a lone pair of electrons and R^4 and R^7 together form a group of the general formula $—(CH_2)—_s$ (wherein s is 1, 2, 3 or 4)] or a tautomer thereof which process comprises reacting a compound of general formula I (wherein R, R^1, R^2, R^3, n and the dotted line are as defined in claim 1, R^{10} and R^{11} together and R^{12} and R^{13} together each form a chemical bond, X and Y each represent sulfur and R^4, R^5, R^6, R^7, R^8 and R^9 each represent an unshared lone pair of electrons a salt being formed between the dianion and a cation) or a tautomer thereof with an alkylene dihalide of the formula $Hlg—(CH_2)_s—Hlg$ (wherein s is as herein defined) whereby the said compound as claimed in claim 1 is obtained.

18. A process as claimed in claim 17 wherein the said cation is an alkali metal cation.

19. A process for the preparation of compounds as claimed in claim 1 (wherein R, R^1, R^2, R^3, R^4, R^5, R^6, X, n and the dotted line are as defined in claim 1, Y represents sulfur, R^8 and R^9 each represent a lone pair of electrons and R^7 represents C_{1-4} alkyl) or a tautomer thereof which process comprises reacting a compound of formula I (wherein R, R^1, R^2, R^3, R^4, R^5, R^6, X, n and the dotted line are as defined in claim 1, R^9 and R^{10} together and R^{11} and R^{12} together each form a chemical bond, R^{13} represents hydrogen, Y represents sulfur and R^7 and R^8 each represent an unshared lone pair of electrons whereby the said compound as claimed in claim 1 is obtained.

20. A process as claimed in claim 19 for the preparation of compounds as claimed in claim 1 (wherein R, R^1, R^2, R^3, and n and the dotted line are as defined in claim 1, R^{10} and R^{11} together and R^{12} and R^{13} together each form a chemical bond, X and Y each represent a sulfur atom, R^5, R^6, R^8 and R^9 each represent an unshared lone pair of electrons and R^4 and R^7, which may be the same or different, each represent C_{1-4} alkyl) or a tautomer thereof wherein a compound of formula I (wherein R, R^1, R^2, R^3, n and the dotted line are as defined in claim 1, R^9 and R^{10} together and R^{11} and R^{12} together each represent a chemical bond, R^{13} represents hydrogen, X and Y each represent a sulfur atom, R^5, R^6, R^7 and R^8 each represent a lone pair of electrons and R^4 represents C_{1-4} alkyl or C_{7-12} aralkyl) or a tautomer thereof is reacted with an alkylating agent whereby the said compounds as claimed in claim 1 are obtained.

21. A process for the preparation of compounds as claimed in claim 1 having the formula



Id

wherein R, R^1, R^2, R^3, n and the dotted lin are as defined in claim 1 which process comprises reacting a compound of formula I (wherein R, R^1, R^2, R^3, n and the dotted lin are as defined in claim 1, R^9 and R^{10} together and R^{11} and R^{12} together each form a chemical bond, R^{13} represents hydrogen, X and Y each represent sulfur, R^5, R^6, R^7, R^8 each represent a lone pair of electrons and R^4 represents C_{1-4} alkyl) with an acid anhydride whereby the said compound as claimed in claim 1 is obtained.

22. A process for the preparation of compounds as claimed in claim 1 wherein [R, R^1, R^2, R^3, n and the dotted line are as defined in claim 1, R^{10} and R^{11} together and R^{12} and R^{13} together each represent a chemical bond, X and Y each represent a nitrogen atom without its lone pair of electrons, R^6 and R^9 each represent a lone pair of electrons, R^5 and R^8 each represent hydrogen or C_{1-4} alkyl and R^4 and R^7 together form an optionally substituted group of the general formula $—(CH_2)s$, (wherein s is 1, 2, 3 or 4)], which process comprises reacting a compound of general formula I (wherein R, R^1, R^2, R^3, n and the dotted line are as defined in claim 1, R^9 and R^{10} together and R^{11} and R^{12} together each form a chemical bond, R^{13} represents hydrogen, X and Y each represent sulfur without its lone pairs of electrons R^5, R^6, R^7 and R^8 each represent a lone pair of electrons and R^4 represents C_{1-4} alkyl) with a diamine of the formula

$$NH_2—(CH_2)_s—NH_2$$

(wherein s is 1, 2, 3 or 4) whereby the said compound as claimed in claim 1 is obtained.

23. A process for the preparation of compounds as claimed in claim 1 (wherein R, R^1, R^2, R^3, n and the dotted line are as defined in claim 1, R^{13} represents hydrogen, R^9 and R^{10} together R^{11} and R^{12} together each form a chemical bond, X and Y each represent an oxygen atom without its lone pairs of electrons, R^5, R^6, R^7, R^8 each represent a lone pair of electrons and R^4 represents C_{1-4} alkyl or C_{7-12}

aralkyl) which process comprises reacting a compound of formula I (wherein R, R^1, R^2, R^3, n and the dotted line are as defined in claim 1, R^9 and R^{10} together and R^{11} and R^{12} together each form a chemical bond, R^{13} represents hydrogen, X, R^4, R^5 and R^6 together represent halogen, Y represents a nitrogen atom without its lone pair of electrons, R^7 represents C_{1-4} alkyl or optionally substituted C_{6-10} aryl, R^8 represents C_{1-4} alkyl and a salt is formed between an anion and the positive nitrogen) with a C_{1-4} alkanol or a C_{7-12} aralkanol whereby the said compound as claimed in claim 1 is obtained.

24. A process as claimed in claim 23 wherein the anion which forms a salt with the positive nitrogen atom is a halide ion.

25. A process for the preparation of compounds as claimed in claim 1 (wherein R, R^1, R^2, R^3, n and the dotted line are as defined in claim 1, R^{13} represents hydrogen, R^9 and R^{10} together and R^{11} and R^{12} together each form a chemical bond, X represents a nitrogen atom without its lone pair of electrons, Y represents an oxygen atom without its lone pair of electrons, and R^6, R^7 and R^8 each represent a lone pair of electrons, R^4 represents C_{1-4} alkyl or optionally substituted C_{6-10} aryl and R^5 represents C_{1-4} alkyl) which process comprises reacting a compound of formula I (wherein R, R^1, R^2, R^3, n and the dotted line are as defined in claim 1, R^9 and R^{10} together and R^{11} and R^{12} together form a chemical bond, R^{13} represents hydrogen, X, R^4, R^5 and R^6 together represent halogen, Y represents a nitrogen atom without its lone pair of electrons, R^7 represents C_{1-4} alkyl or optionally substituted C_{6-10} aryl, R^8 represents C_{1-4} alkyl and a salt is formed between an anion and the positive nitrogen atom) with a water-containing alcohol whereby the said compound as claimed in claim 1 is obtained.

26. A process as claimed in claim 25 wherein the anion which forms a salt with the positive nitrogen atom is a halide ion.

27. A process for the preparation of compounds as claimed in claim 1 (wherein R, R^1, R^2, R^3, n and the dotted line are as defined in claim 1, R^9 and R^{10} together and R^{11} and R^{12} together each form a chemical bond, R^{13} represents hydrogen, X and Y each represents a nitrogen atom without its lone pair of electrons, R^4 represents C_{1-4} alkyl, optionally substituted C_{6-10} aryl or optionally substituted heteroaryl, R^5 represents hydrogen or C_{1-4} alkyl, R^6 represents a lone pair of electrons, R^7 represents C_{1-4} alkyl or optionally substituted C_{6-10} aryl, R^8 represents C_{1-4} alkyl, and a salt is formed between an anion and the positive nitrogen) which process comprises reacting a compound of formula I (wherein R, R^1, R^2, R^4, n and the dotted line are as defined in claim 1, R^9 and R^{10} together and R^{11} and R^{12} together each form a chemical bond, R^{13} is hydrogen, X, R^4, R^5 and R^6 together represents halogen, Y represents a nitrogen atom without its lone pair of electrons, R^7 represents C_{1-4} alkyl or optionally substituted C_{6-10} aryl, R^8 represents C_{1-4} alkyl and an anion forms a salt with the positive nitrogen) with a primary or secondary amine whereby the said compound as claimed in claim 1 is obtained.

28. A process as claimed in claim 27 wherein a compound of formula I is used in which the anion which forms a salt with the positive nitrogen atom is a halide ion.

29. A process for the preparation of compounds as claimed in claim 1 [wherein R, R^1, R^2, R^3, n and the dotted line are as defined in claim 1, R^{10} and R^{11} together and R^{12} and R^{13} together each form a chemical bond, X and Y each represent a nitrogen atom without its lone pair of electrons, R^6 and R^9 each represent a lone pair of electrons, R^5 and R^8 each represent hydrogen or C_{1-4} alkyl and R^4 and R^7 together form an optionally substituted group of the general formula —$(CH_2)_m$, (wherein m is 2, 3 or 4)] which process comprises reacting a compound of the general formula I, (wherein R, R^1, R^2, R^3, n and the dotted line are as defined in claim 1, R^9 and R^{10} together and R^{11} and R^{12} together each form a chemical bond, R^{13} represents hydrogen, X, R^4, R^5 and R^6 represents halogen, Y represents a nitrogen atom without its lone pair of electrons, R^7 represents C_{1-4} alkyl or optionally substituted C_{6-10} aryl and R^8 represents C_{1-4} alkyl, and an anion forms a salt with the positive nitrogen atom) with a diamine of the formula: NH_2—$(CH_2)_m$—NH_2 (wherein m is 2, 3 or 4) whereby the said compound as claimed in claim 1 is obtained.

30. A process as claimed in claim 29 wherein a compound of formula I is used in which the anion which forms a salt with the positive nitrogen atom is a halide ion.

31. A process as claimed in any one of claims 12 to 30 wherein a compound of formula I is obtained and converted into a salt thereof.

32. A process as claimed in any one of claims 12 to 30 wherein a salt of a compound of formula I is obtained and converted into a compound of formula I.

33. A process as claimed in any one of claims 12 to 32 wherein the compound of formula I or a salt thereof in racemic form is converted into its optically active isomers.

34. A process as claimed in any one of claims 12 to 33 substantially as herein described.

35. A process for the preparation of compounds as claimed in claim 1 substantially as herein described in any one of the Examples.

36. Compounds as claimed in claim 1 when prepared by a process as claimed in any one of claims 12 to 35.

37. Pharmaceutical compositions comprising as active ingredient at least one compound of formula I, as defined in claim 1, or a physiologically compatible salt thereof in association with a pharmaceutical carrier or excipient.

38. Each and every novel composition, compound or process herein described.

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